

e) Z" is >CH<sub>2</sub>, >C=O, >C(H)-OH, >C=N-OH, >C=N-OR<sub>5</sub>, >C(H)-C≡N, or >C(H)-NR<sub>5</sub>R<sub>5</sub>, wherein each R<sub>5</sub> is independently hydrogen, an alkyl or branched alkyl with up to 10 carbons or aralkyl;  
with the proviso that if R<sub>b</sub> is H, R<sub>o</sub> is H, Z' is >COH, and Z" is >CH<sub>2</sub>, then R<sub>a</sub> is not -OCH<sub>2</sub>CF<sub>3</sub>.

**REMARKS**

Claims 1-4 and 6-30 are pending and as a result of the previous Restriction Requirement, Claims 15-28 were withdrawn from consideration as a non-elected invention. Therefore, Claims 1-4, 6-14, and 29-30 are currently under consideration. According to the Office Action of November 29, 2002, the Examiner has considered only Claims 1, 6, 12, and 30 of the elected invention, and has not considered Claims drawn to non-elected species; however these claims remain pending.

**Claim Rejections under 35 U.S.C. § 102(e) in View of Sachdeva et al.**

Claims 1, 6, 12, and 30 were rejected in the Office Action of November 29, 2002, as being anticipated under 35 U.S.C. § 102(e) by U.S. Patent No. 6,054,598 to Sachdeva et al. ("Sachdeva"). It is the Examiner's position that Sachdeva discloses both 2-ethoxyestradiol (R<sub>a</sub> is -OCH<sub>2</sub>CH<sub>3</sub>) and 2-(2',2',2'-trifluoroethoxy)estradiol (R<sub>a</sub> is -OCH<sub>2</sub>CF<sub>3</sub>) and therefore anticipates these claims. Applicants respectfully assert that this rejection has been obviated for each of Claims 1, 6, 12, and 30 by the amendments herein, as follows.

Claim 1 is amended herein to recite the proviso that if R<sub>b</sub> is H, R<sub>o</sub> is H, Z' is >COH, >C-R<sub>g</sub> is >C(H)-OH, and Z" is >CH<sub>2</sub>, then R<sub>a</sub> is not -OCH<sub>2</sub>CF<sub>3</sub>. This proviso therefore, excludes 2-(2',2',2'-trifluoroethoxy)estradiol (R<sub>a</sub> is -OCH<sub>2</sub>CF<sub>3</sub>) along with 2-methoxyestradiol and 2-ethoxyestradiol which are already excluded by the proviso of this claim.

Claims 6 and 12 are cancelled by the amendment herein, thereby obviating the rejection of these claims in view of Sachdeva.

Claim 30 is amended herein to recite the proviso that if R<sub>b</sub> is H, R<sub>o</sub> is H, Z' is >COH, >C-R<sub>g</sub> is >C(H)-OH, and Z" is >CH<sub>2</sub>, then R<sub>a</sub> is not -OCH<sub>2</sub>CF<sub>3</sub>. This proviso excludes 2-(2',2',2'-trifluoroethoxy)estradiol (R<sub>a</sub> is -OCH<sub>2</sub>CF<sub>3</sub>) from this claim. The selection of R<sub>a</sub> = OCH<sub>3</sub> is not a possible option for R<sub>a</sub> in Claim 30.

Finally, the proviso feature ">C-R<sub>g</sub> is >C(H)-OH" has been removed from Claim 1 for clarity, because this selection is the only possible choice for >C-R<sub>g</sub> in Claim 1, and is therefore not necessary in the proviso.

Applicants respectfully assert that this rejection has been obviated for each of Claims 1, 6, 12, and 30 by the amendments herein, and therefore request withdrawal of this rejection and allowance of these claims.

**Claim Rejections under 35 U.S.C. § 102(e) in View of D'Amato et al.**

Claims 1, 6, 12, and 30 also appear to be rejected in the November 29, 2002, Office Action as being anticipated under 35 U.S.C. § 102(e) by U.S. Patent No. 5,504,074 to D'Amato et al. ("D'Amato"). It appears to be the Examiner's position that these claims are anticipated by the first two compounds of Table 2, namely, 2-

methoxyestradiol and 2-methoxyestrone. The Examiner also cites Table 1, lines 32, 37, 38 and 41 (column 8) against Claims 1, 6, 12, and 30. Applicants note that this rejection was fully addressed in their response filed June 13, 2002, however in order to expedite examination of this application, Applicants will repeat their arguments.

Applicants note, as they did in their response filed June 13, 2002, that the specific compounds of D'Amato's Table 1 to which the Examiner refers can not be determined unambiguously. However, it is Applicants' belief that the Examiner refers to the following species of Table 1: 2-methoxyestradiol, estradiol, estrone, and 2-methoxyestradiol-3-O-methylether. Applicants respectfully traverse this rejection with respect to Claims 1 and 30 as follows. Further, Applicants' cancellation of Claims 6 and 12 has obviated this rejection with respect to these claims.

2-Methoxyestradiol. As amended, Claim 1 recites the proviso that if R<sub>b</sub> is H, R<sub>0</sub> is H, Z' is >COH, and Z" is >CH<sub>2</sub>, then R<sub>a</sub> is neither -OCH<sub>3</sub>, -OCH<sub>2</sub>CF<sub>3</sub>, nor -OCH<sub>2</sub>CH<sub>3</sub>. This proviso specifically excludes 2-methoxyestradiol from Claim 1, while the definition of R<sub>a</sub> = -OCH<sub>3</sub> is not possible in 30. Therefore, neither Claims 1 nor 30 read on this compound in Table 1 of D'Amato.

Estradiol. This compound requires R<sub>a</sub> to be a hydrogen atom, which is bonded to the C2 position of the steroid A-ring. Applicants respectfully note that neither Claim 1 nor 30 defines R<sub>a</sub> as hydrogen, therefore these claims are not anticipated by this compound in Table 1 of D'Amato.

Estrone. This compound also requires R<sub>a</sub> to be a hydrogen atom, which is bonded to the C2 position of the steroid structure. Applicants respectfully note that

neither Claim 1 nor 30 defines R<sub>a</sub> as hydrogen, therefore these claims are not anticipated by this compound in Table 1 of D'Amato.

2-Methoxyestradiol-3-O-methylether. This compound requires Z' to be >CO-CH<sub>3</sub>, in which a methyl ether moiety is bonded at the C3 position of the steroid structure. Applicants respectfully note that neither Claim 1 nor 30 defines Z' as >CO-CH<sub>3</sub>, therefore these claims are not anticipated by this compound in Table 1 of D'Amato.

Applicants maintain that none of the cited compounds in Table 1 of D'Amato anticipate Claims 1 or 30, and accordingly, Applicants respectfully request withdrawal of this rejection, and allowance of these claims.

**Claim Rejections under 35 U.S.C. § 102(b) in View of Ram et al.**

Claims 1, 6, and 30 were rejected in the Office Action of November 29, 2002, as being anticipated under 35 U.S.C. § 102(b) by U.S. Patent No. 6,136,992 to Ram et al. ("Ram"). It is the Examiner's position that Ram discloses 2-(2',2',2'-trifluoroethoxy)estradiol (R<sub>a</sub> is -OCH<sub>2</sub>CF<sub>3</sub>) and therefore anticipates these claims.

Applicants respectfully assert that Ram does not constitute prior art under 35 U.S.C. § 102(b). The issue date of U.S. Patent No. 6,136,992 to Ram is October 24, 2000, which is after the filing date of the present application. The present application is a continuation of U.S. Patent Application Serial No. 09/154,322, filed September 16, 1998, which claims the benefit of U.S. Provisional Application No. 60/059,916, filed September 24, 1997.

Nonetheless, Applicants respectfully assert that even if this rejection was made on the basis of 35 U.S.C. § 102(e), it has been obviated for each of Claims 1, 6, and 30 by the amendments herein, for the following reasons.

Claim 1 is amended herein to recite the proviso that if R<sub>b</sub> is H, R<sub>O</sub> is H, Z' is >COH, >C-R<sub>g</sub> is >C(H)-OH, and Z" is >CH<sub>2</sub>, then R<sub>a</sub> is not -OCH<sub>2</sub>CF<sub>3</sub>. This proviso therefore, excludes 2-(2',2',2'-trifluoroethoxy)estradiol (R<sub>a</sub> is -OCH<sub>2</sub>CF<sub>3</sub>) along with 2-methoxyestradiol and 2-ethoxyestradiol which are already excluded by the proviso of this claim.

Claim 6 is cancelled by the amendment herein, thereby obviating any rejection of this claim in view of Ram.

Claim 30 is amended herein to recite the proviso that if R<sub>b</sub> is H, R<sub>O</sub> is H, Z' is >COH, >C-R<sub>g</sub> is >C(H)-OH, and Z" is >CH<sub>2</sub>, then R<sub>a</sub> is not -OCH<sub>2</sub>CF<sub>3</sub>. This proviso excludes 2-(2',2',2'-trifluoroethoxy)estradiol (R<sub>a</sub> is -OCH<sub>2</sub>CF<sub>3</sub>) from this claim.

Applicants respectfully assert that any rejection in view of Ram has been obviated for each of Claims 1, 6, and 30 by the amendments herein, and therefore request withdrawal of this rejection and allowance of these claims.

#### **Claim Rejections under 35 U.S.C. § 112, First Paragraph**

Claims 1, 6, 12, and 30 were rejected in the Office Action of November 29, 2002, as being non-enabled under 35 U.S.C. § 112, first paragraph. It is the Examiner's position that the proviso related to disclaimed compounds of Claims 1 and 30 has no support in the disclosure, and therefore that this proviso constitutes new matter.

Claims 6 and 12 are cancelled by the amendment herein, thereby obviating the rejection of these claims under 35 U.S.C. § 112, first paragraph. Applicants respectfully traverse this rejection for Claims 1 and 30 for the following reasons.

Applicants have searched the MPEP with respect to provisos which exclude subject matter, such as those of Claims 1 and 30, and have found no section that prohibits their use. As set forth in MPEP § 2173.05(i), “[i]f alternative elements are positively recited in the specification, they may be **explicitly excluded** in the claims.” (Emphasis added.) Applicants respectfully maintain that alternative elements **are** positively recited in the specification, as alternative definitions of R<sub>a</sub> provided therein. *See*, for example, specification page 15, lines 9-12, and in the individual compounds disclosed in Table 3, page 18 and in Table 1, page 13. Accordingly, Applicants respectfully assert that any of these alternative definitions of R<sub>a</sub> may be **explicitly excluded** in the claims according to MPEP § 2173.05(i), as Applicants have done in Claims 1 and 30.

The only requirement of the MPEP for a proviso to meet the requirements of 35 U.S.C. § 112, first paragraph, is that “[a]ny claim containing a negative limitation *which does not have basis in the original disclosure* should be rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement.” Emphasis added; MPEP § 2173.05(i). Applicants respectfully assert that the individual features of Claims 1 and 30, namely, the **alternative definitions of R<sub>a</sub>**, **have a basis in the original disclosure**. (*See*, for example, specification page 15, lines 9-12; Table 3, page 18; Table 1, page 13. ) The lack of a literal basis for a proviso, by itself, is **not**

sufficient to establish a *prima facie* case for lack descriptive support. MPEP § 2173.05(i); *Ex parte Parks* 30 USPQ2d 1234, 1236 (Bd. Pat. App. & Inter. 1993).

The Federal Circuit has addressed this specific § 112, first paragraph issue in *In re Johnson and Farnham* 194 USPQ 187 (CCPA 1977), where the Court posed, “[t]he only inquiry is whether, after exclusion from the original claim of two species specifically disclosed in the 1963 application, the 1963 disclosure satisfies § 112, first paragraph, for the ‘limited genus’ now claimed.” The *In re Johnson* Court held that the original claim, *with two species excepted out*, satisfied the requirements of 35 U.S.C. § 112, first paragraph, noting that, “...appellants are merely excising the invention of another, to which they are not entitled, and are not creating an ‘artificial subgenus’ or claiming ‘new matter.’” *In re Johnson* at 196.

Applicants respectfully maintain that, for the reasons provided herein and in *In re Johnson*, the provisos of Claims 1 and 30 that remove *some* compounds do not introduce new matter into these claims. Instead, the provisos of Claims 1 and 30 merely reflect the Applicants’ “claiming less than the full scope of [their] disclosure.” *In re Johnson* at 196; emphasis in original. Applicants respectfully assert that patent applicants frequently discover during the course of prosecution that only a part of what they originally claimed is patentable, but “[i]t is for the inventor to decide what *bounds* of protection he will seek.” *In re Johnson* at 196; emphasis in original.

Accordingly, Applicants respectfully assert that Claims 1 and 30 are fully enabled under 35 U.S.C. § 112, first paragraph, and request withdrawal of this rejection and allowance of these claims.

**Claim Rejections under 35 U.S.C. § 112, Second Paragraph**

Claims 1, 6, 12, and 30 were rejected in the Office Action of November 29, 2002, as being indefinite under 35 U.S.C. § 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which applicant regards as his invention. It is the Examiner's position that the feature >C-R<sub>2</sub>-OH in Claims 1 and 30 is unclear, and clarification is required.

Claims 6 and 12 are cancelled by the amendment herein, thereby obviating any rejection of these claims under 35 U.S.C. § 112, Second Paragraph.

The claim feature >C-R<sub>2</sub>-OH appears in Claims 1 and 30 in the definition of Z', wherein R<sub>2</sub> is defined as an alkyl or branched alkyl with up to 10 carbons or aralkyl. Thus, R<sub>2</sub> constitutes an alkyl, branched alkyl, or aralkyl linker between the benzene ring carbon (specified as >C) and the hydroxy group. Examples of >C-R<sub>2</sub>-OH groups that fall into this definition include, but are not limited to >CCH<sub>2</sub>OH, >CCH<sub>2</sub>CH<sub>2</sub>OH, >CCH<sub>2</sub>CH(CH<sub>3</sub>)OH, >CCH<sub>2</sub>(4-C<sub>6</sub>H<sub>4</sub>OH), >CCH<sub>2</sub>(2-C<sub>6</sub>H<sub>4</sub>OH), and the like. Support for this claim feature is found in the specification on page 15, lines 14-15, and in Table 1 page 13.

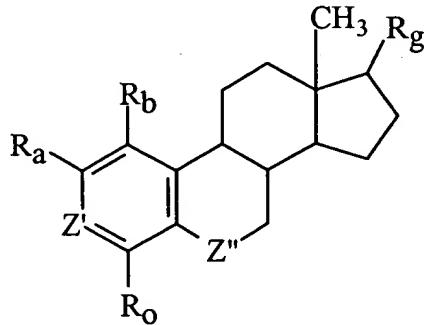
Accordingly, Applicants respectfully assert that Claims 1 and 30 are definite under 35 U.S.C. § 112, second paragraph, and request withdrawal of this rejection and allowance of these claims.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Amendments in the Claims

In accordance with 37 C.F.R. § 1.121(c), the following version of the rewritten claim shows all the changes made by the foregoing amendment relative to the previous version of that claim.

1. (Thrice Amended) A compound of the general formula:



wherein:

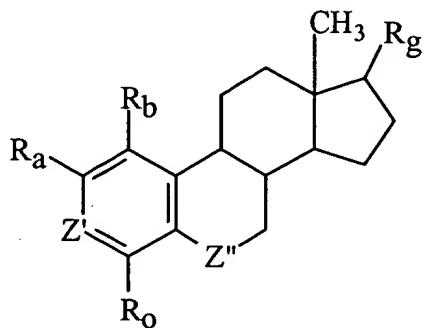
- a) R<sub>b</sub> and R<sub>o</sub> are independently -H, -Cl, -Br, -I, -F, -CN, lower alkyl, -OH, -CH<sub>2</sub>-OH, -NH<sub>2</sub>; or N(R<sub>6</sub>)(R<sub>7</sub>), wherein R<sub>6</sub> and R<sub>7</sub> are independently hydrogen or an alkyl or branched alkyl with up to 6 carbons;
- b) R<sub>a</sub> is -N<sub>3</sub>, -C≡N, -C≡C-R, -CH=CH-R, -R-CH=CH<sub>2</sub>, -C≡CH, -O-R, -R-R<sub>1</sub>, or -O-R-R<sub>1</sub> where R is a straight or branched alkyl with up to 10 carbons or aralkyl, and R<sub>1</sub> is -OH, -NH<sub>2</sub>, -Cl, -Br, -I, -F or CF<sub>3</sub>;
- c) Z' is >CH, >COH, or >C-R<sub>2</sub>-OH, where R<sub>2</sub> is an alkyl or branched alkyl with up to 10 carbons or aralkyl;

d) >C-R<sub>g</sub> is >C(H)-OH; and

e) Z" is >CH<sub>2</sub>, >C=O, >C(H)-OH, >C=N-OR<sub>5</sub>, >C(H)-C≡N, or >C(H)-NR<sub>5</sub>R<sub>5</sub>, wherein each R<sub>5</sub> is independently hydrogen, an alkyl or branched alkyl with up to 10 carbons or aralkyl;  
with the proviso that if R<sub>b</sub> is H, R<sub>o</sub> is H, Z' is >COH, [>C-R<sub>g</sub> is >C(H)-OH,] and Z" is >CH<sub>2</sub>, then R<sub>a</sub> is neither -OCH<sub>3</sub>, -OCH<sub>2</sub>CF<sub>3</sub>, nor -OCH<sub>2</sub>CH<sub>3</sub>.

30. (Twice Amended)

A compound of the general formula:



wherein:

a) R<sub>b</sub> and R<sub>o</sub> are independently -H, -Cl, -Br, -I, -F, -CN, lower alkyl, -OH, -CH<sub>2</sub>-OH, -NH<sub>2</sub>; or N(R<sub>6</sub>)(R<sub>7</sub>), wherein R<sub>6</sub> and R<sub>7</sub> are independently hydrogen or an alkyl or branched alkyl with up to 6 carbons;

b) R<sub>a</sub> is -O-R-R<sub>1</sub> where R is a straight or branched alkyl with up to 10 carbons or aralkyl, and R<sub>1</sub> is -OH, -NH<sub>2</sub>, -Cl, -Br, -I, -F or CF<sub>3</sub>;

c)  $Z'$  is  $>\text{CH}$ ,  $>\text{COH}$ , or  $>\text{C}-\text{R}_2-\text{OH}$ , where  $\text{R}_2$  is an alkyl or branched alkyl with up to 10 carbons or aralkyl;

d)  $>\text{C}-\text{R}_g$  is  $>\text{C}(\text{H})-\text{OH}$ ; and

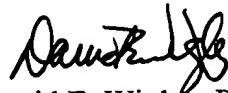
e)  $Z''$  is  $>\text{CH}_2$ ,  $>\text{C=O}$ ,  $>\text{C}(\text{H})-\text{OH}$ ,  $>\text{C=N-OH}$ ,  $>\text{C=N-OR}_5$ ,  $>\text{C}(\text{H})-\text{C}\equiv\text{N}$ , or  $>\text{C}(\text{H})-\text{NR}_5\text{R}_5$ , wherein each  $\text{R}_5$  is independently hydrogen, an alkyl or branched alkyl with up to 10 carbons or aralkyl;[.]

with the proviso that if  $\text{R}_b$  is H,  $\text{R}_0$  is H,  $Z'$  is  $>\text{COH}$ , and  $Z''$  is  $>\text{CH}_2$ , then  $\text{R}_g$  is not  $-\text{OCH}_2\text{CF}_3$ .

Conclusion

In light of the above amendments and remarks, Applicants maintain that the present application is in condition for allowance. Such action is respectfully requested. If the Examiner believes there are any other issues that may be resolved by telephone interview, a telephone call to the undersigned attorney at (404) 815-6500 is courteously solicited.

Respectfully submitted,



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